IN THE CLAIMS

1 (withdrawn): A method for inhibiting bone metastases and metastatic growth in a patient which comprises administering to the patient in need thereof a therapeutically effective amount of an endothelin ET-A receptor antagonist.

2 (withdrawn): The method of Claim 1 wherein the bone metastases are osteoblastic.

3 (withdrawn): The method of Claim 2 wherein the osteoblastic bone metastases result from the spread of a primary cancer selected from breast, prostate, lung, kidney, thyroid, myeloma, lymphoma, sarcoma, osteosarcoma, and ovarian.

4 (withdrawn): The method of Claim 3 wherein the primary cancer is prostate cancer and the patient is male.

5 (withdrawn): The method of Claim 1 which additionally comprises co-administeration of an anticancer drug.

6 (withdrawn): The method of Claim 5 wherein the anticancer drug agent is selected from leuprolide, goserelin, bicalutamide, nilutamide, flutamide, vitamin D, vitamin D analogues, estrogen, estrogen analogues, prednisone, hydrocortisone, ketoconazole, cyproterone acetate, and progesterone.

7 (withdrawn): The method of Claim 1 which additionally comprises the administeration of radiation therapy.

8 (withdrawn): The method of Claim 1 which additionally comprises the administeration of at least one therapeutic agent which impedes net bone loss.

9 (withdrawn): The method of Claim 8 wherein the therapeutic agent is a bisphosphonate.

10 (withdrawn): The method of Claim 1 wherein the endothelin antagonist is an ET_A-selective endothelin antagonist.

11 (withdrawn): A method for the inhibition of bone loss in a patient which comprises administering to the patient in need thereof a therapeutically effective amount of an endothelin ET-A receptor antagonist.

12 (withdrawn): The method of Claim 11 wherein the patient has cancer.

13 (withdrawn): The method of Claim 11 wherein the cancer is prostate cancer and the patient is male.

14 (withdrawn): The method of Claim 11 which additionally comprises the administeration of at least one therapeutic agent which impedes net bone loss.

15 (withdrawn): The method of Claim 14 wherein the therapeutic agent is a bisphosphonate.

16 (withdrawn): A method for the reduction of cancer-related pain in a patient which comprises administering to the patient in need thereof a therapeutically effective amount of an endothelin ET-A receptor antagonist.

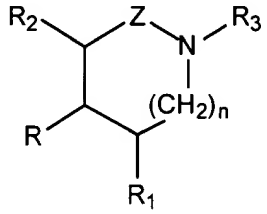
17 (withdrawn): The method of Claim 16 wherein the cancer is prostate cancer and the patient is male.

18 (withdrawn): The method of Claim 16 which additionally comprises the administeration of an anticancer drug.

19 (withdrawn): The method of Claim 18 wherein the anticancer drug is selected from leuprolide, goserelin, bicalutamide, nilutamide, flutamide, vitamin D, vitamin D analogues, estrogen, estrogen analogues, prednisone, hydrocortisone, ketoconazole, cyproterone acetate, and progesterone.

20 (withdrawn): The method of Claim 17 which additionally comprises the administeration of radiation therapy.

21 (withdrawn): A method for inhibiting bone metastases in a patient which comprises administering to the patient in need thereof a therapeutically effective amount of a compound of formula I:



I

wherein

R is $-(CH_2)_m-W$;

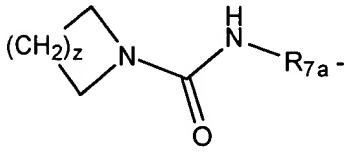
Z is selected from $-C(R_{18})(R_{19})-$ and $-C(O)-$;

R_1 and R_2 are independently selected from hydrogen, loweralkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonylalkyl, hydroxyalkyl, haloalkyl, haloalkoxyalkyl, alkoxyalkoxyalkyl, thioalkoxyalkoxyalkyl, cycloalkyl, cycloalkylalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, aminocarbonylalkenyl, alkylaminocarbonylalkenyl, dialkylaminocarbonylalkenyl, hydroxyalkenyl, aryl, arylalkyl, aryloxyalkyl, arylalkoxyalkyl, (Nalkanoyl-N-alkyl)aminoalkyl, alkylsulfonylamidoalkyl, heterocyclic, (heterocyclic)alkyl, and $(R_{aa})(R_{bb})N-R_{cc}-$,

with the proviso that one or both of R_1 and R_2 is other than hydrogen;

R_3 is selected from R_4-C(O)-R_5-, R_4-R_{5a}-, R_4-C(O)-R_5-N(R_6)-, R_6-S(O)$_2$-R_7-R_{26}-S(O)-R_{27}-, R_{22}-O-C(O)-R_{23}-, loweralkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, aryloxyalkyl, heterocyclic, (heterocyclic)alkyl, alkoxyalkyl, alkoxyalkoxyalkyl, and R_{13}-C(O)-CH(R_{14})-;

R_4 and R_6 are independently selected from (R_{11})(R_{12})N-, loweralkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclic, (heterocyclic)alkyl, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkenyl, haloalkoxyalkyl, haloalkoxy, alkoxyhaloalkyl, alkylaminoalkyl, dialkylaminoalkyl, alkoxy, and



R_5 is selected from a covalent bond, alkylene, alkenylene, -N(R_{20})-R_8-, -R_{8a}-N(R_{20})-R_8-, -O-R_9-, and

-R_{9a}-O-R_9-;

R_6 is selected from loweralkyl, haloalkyl, alkoxyalkyl, haloalkoxyalkyl, aryl or arylalkyl;

R_7 is a covalent bond, alkylene, alkenylene -N(R_{21})-R_{10}-, and -R_{10a}-N(R_{21})-R_{10}-;

R_8 is selected from alkylene and alkenylene;

R_9 is alkylene;

R_{10} is selected from alkylene and alkenylene;

R_{11} and R_{12} are independently selected from hydrogen, loweralkyl, haloalkyl, alkoxyalkyl, haloalkoxyalkylalkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, heterocyclic, arylalkyl, (heterocyclic)alkyl, hydroxyalkyl, alkoxy, aminoalkyl,trialkylaminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, and carboxyalkyl;

R_{13} is selected from amino, alkylamino and dialkylamino;

R_{14} is selected from aryl and R_{15}-C(O)-;

R_{15} is selected from amino, alkylamino and dialkylamino;

R_{16} is selected from loweralkyl, haloalkyl, aryl and dialkylamino;

R_{17} is loweralkyl;

R_{18} and R_{19} are independently selected from hydrogen and loweralkyl;

R_{20} is selected from hydrogen, loweralkyl, alkenyl, haloalkyl, alkoxyalkyl, haloalkoxyalkyl, cylcoalkyl and cycloalkylalkyl;

R_{21} is selected from hydrogen, loweralkyl, alkenyl, haloalkyl, alkoxyalkyl, haloalkoxyalkyl, aryl and arylalkyl;

R_{22} is selected from a carboxy protecting group and heterocyclic;

R_{23} is selected from covalent bond, alkylene, alkenylene and -N(R_{24})-R_{25}-;

R_{24} is selected from hydrogen and loweralkyl;

R_{25} is alkylene;

R_{26} is selected from loweralkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclic, (heterocyclic)alkyl, alkoxyalkyl and alkoxy substituted haloalkyl;

R_{27} is selected from alkylene and alkenylene;

R_{5a} is selected from alkylene and alkenylene;

R_{7a} is alkylene;

R_{8a} is selected from alkylene and alkenylene;

R_{9a} is alkylene;

R_{10a} is selected from alkylene and alkenylene;

R_{aa} is selected from aryl and arylalkyl;

R_{bb} is selected from hydrogen and alkanoyl;

R_{cc} is alkylene;

m is 0-6;

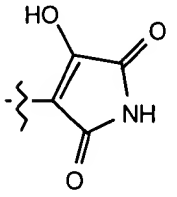
n is 0 or 1;

z is 0-5;

E is selected from hydrogen, loweralkyl and arylalkyl;

G is selected from hydrogen and a carboxy protecting group; and

W is selected from -C(O)$_2$-G; -PO$_3$H$_2$, -P(O)(OH)(E), -CN, -C(O)NHR$_{17}$, alkylaminocarbonyl, dialkylaminocarbonyl, tetrazolyl, hydroxy, alkoxy, sulfonamido, -C(O)NHS(O)$_2$R$_{16}$, -S(O)$_2$NHC(O)R$_{16}$,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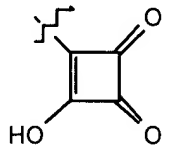
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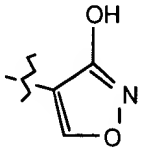
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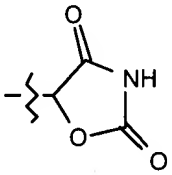
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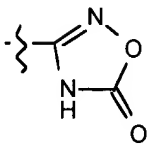
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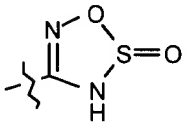
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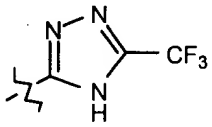
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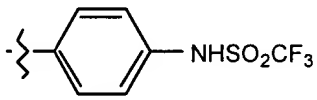
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or a pharmaceutically acceptable salt thereof.

22 (withdrawn): The method of Claim 21 wherein the bone metastases are osteoblastic.

23 (withdrawn): The method of Claim 22 wherein the osteoblastic bone metastases result from the spread of a primary cancer selected from breast, prostate, lung, kidney, thyroid, myeloma, lymphoma, sarcoma, osteosarcoma, and ovarian.

24 (withdrawn): The method of Claim 23 wherein the primary cancer is prostate cancer and the patient is male.

25 (withdrawn): The method of Claim 21 which additionally comprises the administeration of an anticancer drug.

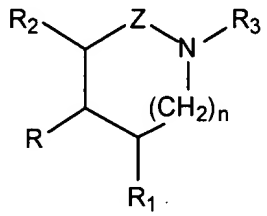
26 (withdrawn): The method of Claim 25 wherein the additional anticancer drug is selected from leuprolide, goserelin, bicalutamide, nilutamide, flutamide, vitamin D, vitamin D analogues, estrogen, estrogen analogues, prednisone, hydrocortisone, ketoconazole, cyproterone acetate, and progesterone.

27 (withdrawn): The method of Claim 21 which additionally comprises the administeration of radiation therapy.

28 (withdrawn): The method of Claim 21 which additionally comprises the administeration of at least one therapeutic agent which impedes net bone loss.

29 (withdrawn): The method of Claim 28 wherein the therapeutic agent is a bisphosphonate.

30 (withdrawn): A method for the inhibition of bone loss in cancer patients which comprises administering to the patient in need thereof a therapeutically effective amount of a compound of formula I:



I

wherein

R is $-(CH_2)_m-W$;

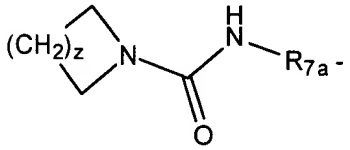
Z is selected from $-C(R_{18})(R_{19})-$ and $-C(O)-$;

R_1 and R_2 are independently selected from hydrogen, loweralkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonylalkyl, hydroxyalkyl, haloalkyl, haloalkoxyalkyl, alkoxyalkoxyalkyl, thioalkoxyalkoxyalkyl, cycloalkyl, cycloalkylalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, aminocarbonylalkenyl, alkylaminocarbonylalkenyl, dialkylaminocarbonylalkenyl, hydroxyalkenyl, aryl, arylalkyl, aryloxyalkyl, arylalkoxyalkyl, (Nalkanoyl-N-alkyl)aminoalkyl, alkylsulfonylamidoalkyl, heterocyclic, (heterocyclic)alkyl, and $(R_{aa})(R_{bb})N-R_{cc}-$,

with the proviso that one or both of R_1 and R_2 is other than hydrogen;

R_3 is selected from R_4-C(O)-R_5-, R_4-R_{5a}-, R_4-C(O)-R_5-N(R_6)-, R_6-S(O)$_2$-R_7-R_{26}-S(O)-R_{27}-, R_{22}-O-C(O)-R_{23}-, loweralkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, aryloxyalkyl, heterocyclic, (heterocyclic)alkyl, alkoxyalkyl, alkoxyalkoxyalkyl, and R_{13}-C(O)-CH(R_{14})-;

R_4 and R_6 are independently selected from (R_{11})(R_{12})N-, loweralkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclic, (heterocyclic)alkyl, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkenyl, haloalkoxyalkyl, haloalkoxy, alkoxyhaloalkyl, alkylaminoalkyl, dialkylaminoalkyl, alkoxy, and



R_5 is selected from a covalent bond, alkylene, alkenylene, -N(R_{20})-R_8-, -R_{8a}-N(R_{20})-R_8-, -O-R_9-, and

-R_{9a}-O-R_9-;

R_6 is selected from loweralkyl, haloalkyl, alkoxyalkyl, haloalkoxyalkyl, aryl or arylalkyl;

R_7 is a covalent bond, alkylene, alkenylene -N(R_{21})-R_{10}-, and -R_{10a}-N(R_{21})-R_{10}-;

R_8 is selected from alkylene and alkenylene;

R_9 is alkylene;

R_{10} is selected from alkylene and alkenylene;

R_{11} and R_{12} are independently selected from hydrogen, loweralkyl, haloalkyl, alkoxyalkyl, haloalkoxyalkylalkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, heterocyclic, arylalkyl, (heterocyclic)alkyl, hydroxyalkyl, alkoxy, aminoalkyl,trialkylaminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, and carboxyalkyl;

R_{13} is selected from amino, alkylamino and dialkylamino;

R_{14} is selected from aryl and R_{15}-C(O)-;

R_{15} is selected from amino, alkylamino and dialkylamino;

R_{16} is selected from loweralkyl, haloalkyl, aryl and dialkylamino;

R_{17} is loweralkyl;

R_{18} and R_{19} are independently selected from hydrogen and loweralkyl;

R_{20} is selected from hydrogen, loweralkyl, alkenyl, haloalkyl, alkoxyalkyl, haloalkoxyalkyl, cylcoalkyl and cycloalkylalkyl;

R_{21} is selected from hydrogen, loweralkyl, alkenyl, haloalkyl, alkoxyalkyl, haloalkoxyalkyl, aryl and arylalkyl;

R_{22} is selected from a carboxy protecting group and heterocyclic;

R_{23} is selected from covalent bond, alkylene, alkenylene and -N(R_{24})-R_{25}-;

R_{24} is selected from hydrogen and loweralkyl;

R_{25} is alkylene;

R_{26} is selected from loweralkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclic, (heterocyclic)alkyl, alkoxyalkyl and alkoxy substituted haloalkyl;

R_{27} is selected from alkylene and alkenylene;

R_{5a} is selected from alkylene and alkenylene;

R_{7a} is alkylene;

R_{8a} is selected from alkylene and alkenylene;

R_{9a} is alkylene;

R_{10a} is selected from alkylene and alkenylene;

R_{aa} is selected from aryl and arylalkyl;

R_{bb} is selected from hydrogen and alkanoyl;

R_{cc} is alkylene;

m is 0-6;

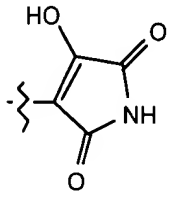
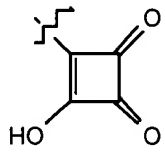
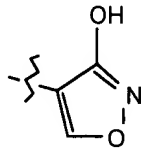
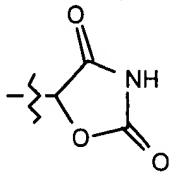
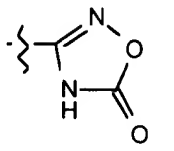
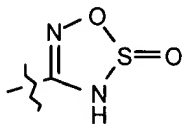
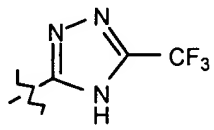
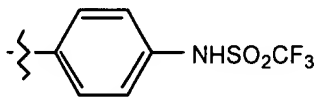
n is 0 or 1;

z is 0-5;

E is selected from hydrogen, loweralkyl and arylalkyl;

G is selected from hydrogen and a carboxy protecting group; and

W is selected from -$C(O)_2$-G; -PO_3H_2, -P(O)(OH)(E), -CN, -$C(O)NHR_{17}$, alkylaminocarbonyl, dialkylaminocarbonyl, tetrazolyl, hydroxy, alkoxy, sulfonamido, -$C(O)NHS(O)_2R_{16}$, -$S(O)_2NHC(O)R_{16}$,

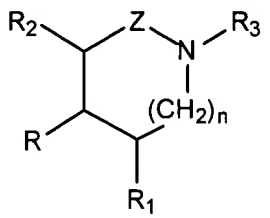
or a pharmaceutically acceptable salt thereof.

31 (withdrawn): The method of Claim 30 wherein the cancer is prostate cancer and the patient is male.

32 (withdrawn): The method of Claim 30 which additionally comprises the administeration of at least one therapeutic agent which impedes net bone loss.

33 (withdrawn): The method of Claim 32 wherein the therapeutic agent is a bisphosphonate.

34 (withdrawn): A method for the reduction of cancer-related pain which comprises administering to a patient in need thereof a therapeutically effective amount of a compound of formula I:



I

wherein

R is $-(CH_2)_m-W$;

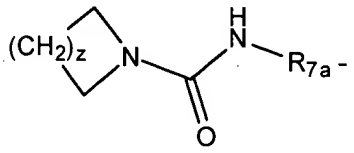
Z is selected from $-C(R_{18})(R_{19})-$ and $-C(O)-$;

R_1 and R_2 are independently selected from hydrogen, loweralkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonylalkyl, hydroxyalkyl, haloalkyl, haloalkoxyalkyl, alkoxyalkoxyalkyl, thioalkoxyalkoxyalkyl, cycloalkyl, cycloalkylalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, aminocarbonylalkenyl, alkylaminocarbonylalkenyl, dialkylaminocarbonylalkenyl, hydroxyalkenyl, aryl, arylalkyl, aryloxyalkyl, arylalkoxyalkyl, (Nalkanoyl-N-alkyl)aminoalkyl, alkylsulfonylamidoalkyl, heterocyclic, (heterocyclic)alkyl, and $(R_{aa})(R_{bb})N-R_{cc}-$,

with the proviso that one or both of R_1 and R_2 is other than hydrogen;

R_3 is selected from $R_4-C(O)-R_5-$, $R_4-R_{5a}-$, $R_4-C(O)-R_5-N(R_6)-$, $R_6-S(O)_2-R_7-$ $R_{26}-S(O)-R_{27}-$, $R_{22}-O-C(O)-R_{23}-$, loweralkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, aryloxyalkyl, heterocyclic, (heterocyclic)alkyl, alkoxyalkyl, alkoxyalkoxyalkyl, and $R_{13}-C(O)-CH(R_{14})-$;

R_4 and R_6 are independently selected from $(R_{11})(R_{12})N-$, loweralkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclic, (heterocyclic)alkyl, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkenyl, haloalkoxyalkyl, haloalkoxy, alkoxyhaloalkyl, alkylaminoalkyl, dialkylaminoalkyl, alkoxy, and



R_5 is selected from a covalent bond, alkylene, alkenylene, $-N(R_{20})-R_8-$, $-R_{8a}-N(R_{20})-R_8-$, $-O-R_9-$, and

$-R_{9a}-O-R_9-$;

R_6 is selected from loweralkyl, haloalkyl, alkoxyalkyl, haloalkoxyalkyl, aryl or arylalkyl;

R_7 is a covalent bond, alkylene, alkenylene -N(R_{21})-R_{10}-, and -R_{10a}-N(R_{21})-R_{10}-;

R_8 is selected from alkylene and alkenylene;

R_9 is alkylene;

R_{10} is selected from alkylene and alkenylene;

R_{11} and R_{12} are independently selected from hydrogen, loweralkyl, haloalkyl, alkoxyalkyl, haloalkoxyalkylalkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, heterocyclic, arylalkyl, (heterocyclic)alkyl, hydroxyalkyl, alkoxy, aminoalkyl,trialkylaminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, and carboxyalkyl;

R_{13} is selected from amino, alkylamino and dialkylamino;

R_{14} is selected from aryl and R_{15}-C(O)-;

R_{15} is selected from amino, alkylamino and dialkylamino;

R_{16} is selected from loweralkyl, haloalkyl, aryl and dialkylamino;

R_{17} is loweralkyl;

R_{18} and R_{19} are independently selected from hydrogen and loweralkyl;

R_{20} is selected from hydrogen, loweralkyl, alkenyl, haloalkyl, alkoxyalkyl, haloalkoxyalkyl, cylcoalkyl and cycloalkylalkyl;

R_{21} is selected from hydrogen, loweralkyl, alkenyl, haloalkyl, alkoxyalkyl, haloalkoxyalkyl, aryl and arylalkyl;

R_{22} is selected from a carboxy protecting group and heterocyclic;

R_{23} is selected from covalent bond, alkylene, alkenylene and -N(R_{24})-R_{25}-;

R_{24} is selected from hydrogen and loweralkyl;

R_{25} is alkylene;

R_{26} is selected from loweralkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclic, (heterocyclic)alkyl, alkoxyalkyl and alkoxy-substituted haloalkyl;

R_{27} is selected from alkylene and alkenylene;

R_{5a} is selected from alkylene and alkenylene;

R_{7a} is alkylene;

R_{8a} is selected from alkylene and alkenylene;

R_{9a} is alkylene;

R_{10a} is selected from alkylene and alkenylene;

R_{aa} is selected from aryl and arylalkyl;

R_{bb} is selected from hydrogen and alkanoyl;

R_{cc} is alkylene;

m is 0-6;

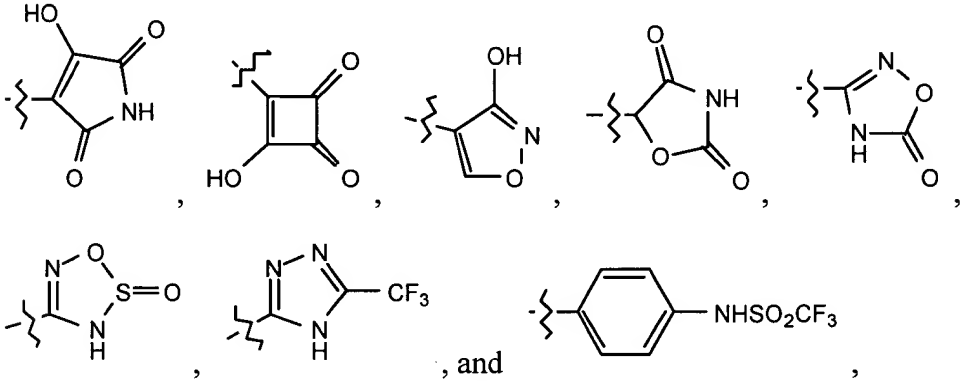
n is 0 or 1;

z is 0-5;

E is selected from hydrogen, loweralkyl and arylalkyl;

G is selected from hydrogen and a carboxy protecting group; and

W is selected from $-C(O)_2-G$; $-PO_3H_2$, -P(O)(OH)(E), -CN, $-C(O)NHR_{17}$, alkylaminocarbonyl, dialkylaminocarbonyl, tetrazolyl, hydroxy, alkoxy, sulfonamido, $-C(O)NHS(O)_2R_{16}$, $-S(O)_2NHC(O)R_{16}$,



, and

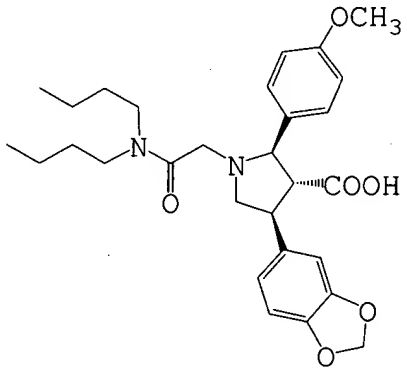
or a pharmaceutically acceptable salt thereof.

35 (withdrawn): The method of Claim 34 wherein the cancer is prostate cancer and the patient is male.

36 (withdrawn): The method of Claim 34 which additionally comprises the administeration of an anticancer drug.

37 (withdrawn): The method of Claim 36 wherein the additional anticancer drug is selected from leuprolide, goserelin, bicalutamide, nilutamide, flutamide, vitamin D, vitamin D analogues, estrogen, estrogen analogues, prednisone, hydrocortisone, ketoconazole, cyproterone acetate, and progesterone.

38 (currently amended): A method for inhibiting bone metastases from prostate cancer in a ~~patient having prostate cancer which comprises~~ human comprising administering thereto ~~to the patient~~ a therapeutically effective amount of a compound of formula III



III,

or a pharmaceutically acceptable salt thereof.

39 (original): The method of Claim 38 wherein the bone metastases are osteoblastic.

40 (withdrawn): The method of Claim 39 wherein the osteoblastic bone metastases result from the spread of a primary cancer selected from breast, prostate, lung, kidney, thyroid, myeloma, lymphoma, sarcoma, osteosarcoma, and ovarian.

41 (withdrawn): The method of Claim 40 wherein the primary cancer is prostate cancer and the patient is male.

42 (currently amended): The method of Claim ~~40~~ 38 which additionally comprises administering an anticancer drug.

43 (original): The method of Claim 42 wherein the anticancer drug is selected from the group consisting of leuprolide, goserelin, bicalutamide, nilutamide, flutamide, vitamin D, vitamin D analogues, estrogen, estrogen analogues, prednisone, hydrocortisone, ketoconazole, cyproterone acetate, and progesterone.

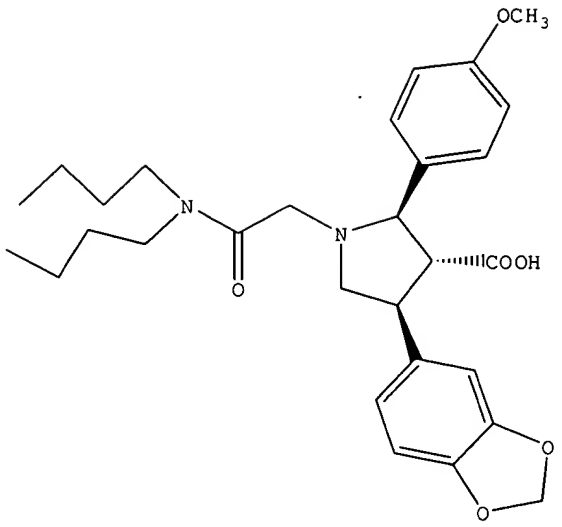
44 (currently amended): The method of Claim ~~40~~ 38 which additionally comprises administering radiation.

45 (currently amended): The method of Claim ~~40~~ 38 which additionally comprises administering at least one therapeutic agent which impedes net bone loss.

46 (original): The method of Claim 45 wherein the therapeutic agent is a bisphosphonate.

47 (withdrawn): The method of Claim 40 wherein the endothelin antagonist is an ET_A-selective endothelin antagonist.

48 (withdrawn): A method for the inhibition of bone loss in cancer patients which comprises administering to the patient in need thereof a therapeutically effective amount of a compound of formula III



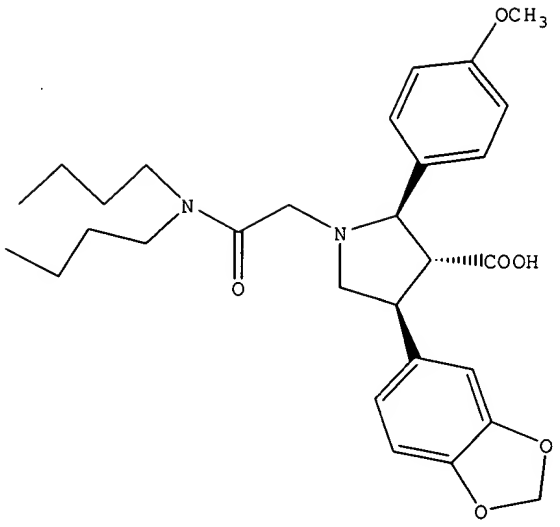
III.

49 (withdrawn): The method of Claim 48 wherein the cancer is prostate cancer and the patient is male.

50 (withdrawn): The method of Claim 48 which additionally comprises the administeration of at least one therapeutic agent which impedes net bone loss.

51 (withdrawn): The method of Claim 50 wherein therapeutic agent is a bisphosphonate.

52 (withdrawn): A method for the reduction of cancer-related pain which comprises administering to a patient in need thereof a therapeutically effective amount of a compound of formula III



III.

53 (withdrawn): The method of Claim 52 wherein the cancer is prostate cancer and the patient is male.

54 (withdrawn): The method of Claim 52 which additionally comprises the administeration of an anticancer drug.

55 (withdrawn): The method of Claim 54 wherein the anticancer drug is selected from leuprolide, goserelin, bicalutamide, nilutamide, flutamide, vitamin D, vitamin D analogues, estrogen, estrogen analogues, prednisone, hydrocortisone, ketoconazole, cyproterone acetate, and progesterone.

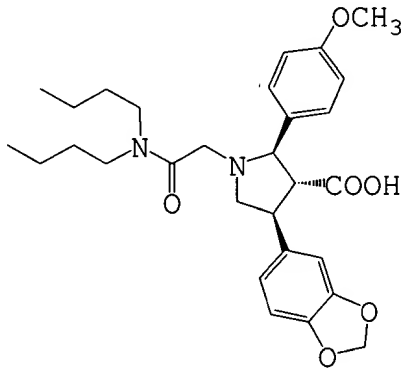
56 (cancelled)

57 (withdrawn): A method for inhibiting metastatic growth in a patient which comprises administring to the patient in need thereof a therapeutically effective amount of an endothelin ET-A receptor antagonist.

58 (withdrawn): A method for inhibiting bone turnover in a patient which comprises administring to the patient in need thereof a therapeutically effective amount of an endothelin ET-A receptor antagonist.

59-64 (canceled)

65 (amended): A method for inhibiting metastatic growth from prostate cancer in a ~~patient having prostate cancer which comprises~~ human comprising administering thereto ~~to the patient~~ a therapeutically effective amount of a compound of formula III



III,

or a pharmaceutically acceptable salt thereof.

66 (original): The method of Claim 65 wherein the ~~bone metastases are~~ metastatic growth is osteoblastic metastatic growth.

67 (original): The method of Claim 65 which additionally comprises administering an anticancer drug.

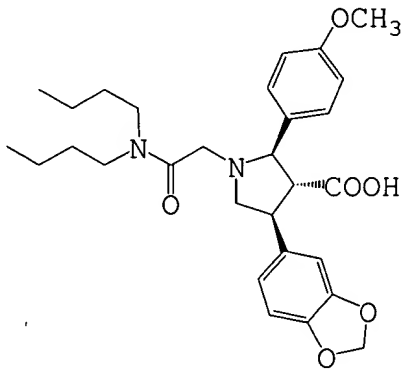
68 (original): The method of Claim 67 wherein the anticancer drug is selected from the group consisting of leuprolide, goserelin, bicalutamide, nilutamide, flutamide, vitamin D, vitamin D analogues, estrogen, estrogen analogues, prednisone, hydrocortisone, ketoconazole, cyproterone acetate, and progesterone.

69 (original): The method of Claim 65 which additionally comprises administering radiation.

70 (original): The method of Claim 65 which additionally comprises administering at least one therapeutic agent which impedes net bone loss.

71 (original): The method of Claim 70 wherein the therapeutic agent is a bisphosphonate.

72 (new): A method for inhibiting osteoblastic bone metastases from prostate cancer in a human comprising administering thereto a therapeutically effective amount of a compound of formula III



III,

or a pharmaceutically acceptable salt thereof.

73 (new): The method of Claim 72 which additionally comprises administering an anticancer drug.

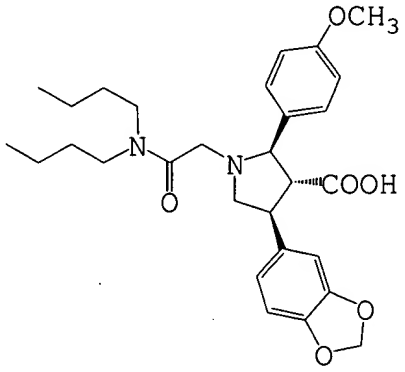
74 (new): The method of Claim 73 wherein the anticancer drug is selected from the group consisting of leuprolide, goserelin, bicalutamide, nilutamide, flutamide, vitamin D, vitamin D analogues, estrogen, estrogen analogues, prednisone, hydrocortisone, ketoconazole, cyproterone acetate, and progesterone.

75 (new): The method of Claim 72 which additionally comprises administering radiation.

76 (new): The method of Claim 72 which additionally comprises administering at least one therapeutic agent which impedes net bone loss.

77 (original): The method of Claim 76 wherein the therapeutic agent is a bisphosphonate.

78 (new): A method for inhibiting osteoblastic metastatic growth from prostate cancer in a human comprising administering thereto a therapeutically effective amount of a compound of formula III



III,

or a pharmaceutically acceptable salt thereof.

79 (new): The method of Claim 78 which additionally comprises administering an anticancer drug.

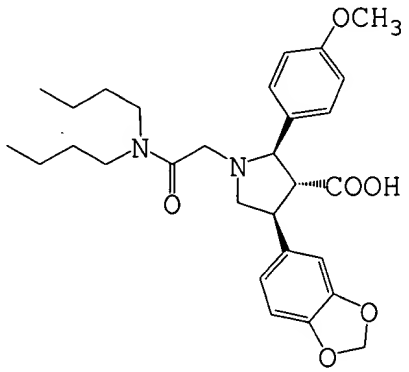
80 (new): The method of Claim 79 wherein the anticancer drug is selected from the group consisting of leuprolide, goserelin, bicalutamide, nilutamide, flutamide, vitamin D, vitamin D analogues, estrogen, estrogen analogues, prednisone, hydrocortisone, ketoconazole, cyproterone acetate, and progesterone.

81 (new): The method of Claim 78 which additionally comprises administering radiation.

82 (new): The method of Claim 78 which additionally comprises administering at least one therapeutic agent which impedes net bone loss.

83 (original): The method of Claim 82 wherein the therapeutic agent is a bisphosphonate.

84 (new): A method for inhibiting bone metastases from prostate cancer in a human comprising administering thereto a therapeutically effective amount of the hydrochloride salt of a compound of formula III



III.

85 (new): The method of Claim 84 wherein the bone metastases are osteoblastic.

86 (new): The method of Claim 84 which additionally comprises administering an

anticancer drug.

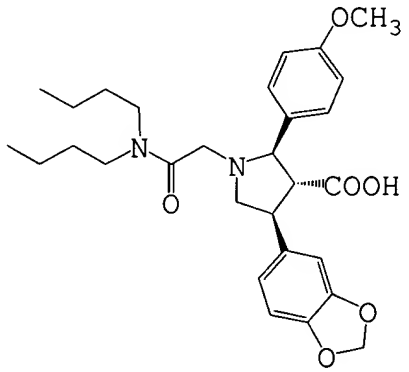
87 (new): The method of Claim 86 wherein the anticancer drug is selected from the group consisting of leuprolide, goserelin, bicalutamide, nilutamide, flutamide, vitamin D, vitamin D analogues, estrogen, estrogen analogues, prednisone, hydrocortisone, ketoconazole, cyproterone acetate, and progesterone.

88 (new): The method of Claim 84 which additionally comprises administering radiation.

89 (new): The method of Claim 84 which additionally comprises administering at least one therapeutic agent which impedes net bone loss.

90 (new): The method of Claim 89 wherein the therapeutic agent is a bisphosphonate.

91 (new): A method for inhibiting metastatic growth from prostate cancer in a human comprising administering thereto a therapeutically effective amount of the hydrochloride salt of a compound of formula III



III.

92 (new): The method of Claim 91 wherein the metastatic growth is osteoblastic metastatic growth.

93 (new): The method of Claim 91 which additionally comprises administering an anticancer drug.

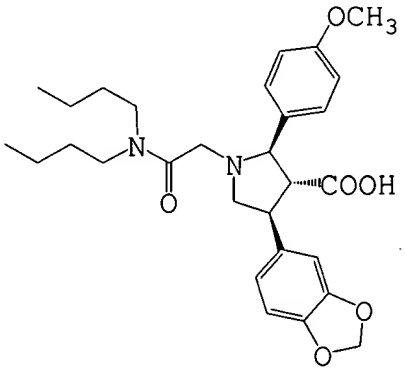
94 (new): The method of Claim 93 wherein the anticancer drug is selected from the group consisting of leuprolide, goserelin, bicalutamide, nilutamide, flutamide, vitamin D, vitamin D analogues, estrogen, estrogen analogues, prednisone, hydrocortisone, ketoconazole, cyproterone acetate, and progesterone.

95 (new): The method of Claim 91 which additionally comprises administering radiation.

96 (new): The method of Claim 91 which additionally comprises administering at least one therapeutic agent which impedes net bone loss.

97 (new): The method of Claim 96 wherein the therapeutic agent is a bisphosphonate.

98 (new): A method for inhibiting osteoblastic bone metastases from prostate cancer in a human comprising administering thereto a therapeutically effective amount of the hydrochloride salt of a compound of formula III



III.

99 (new): The method of Claim 98 which additionally comprises administering an anticancer drug.

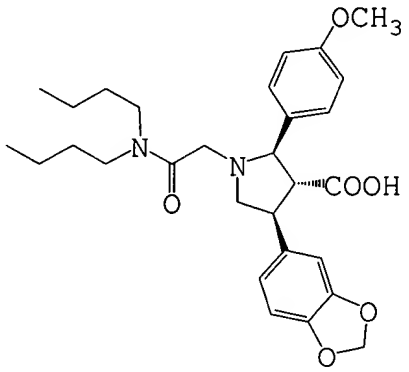
100 (new): The method of Claim 99 wherein the anticancer drug is selected from the group consisting of leuprolide, goserelin, bicalutamide, nilutamide, flutamide, vitamin D, vitamin D analogues, estrogen, estrogen analogues, prednisone, hydrocortisone, ketoconazole, cyproterone acetate, and progesterone.

101 (new): The method of Claim 98 which additionally comprises administering radiation.

102 (new): The method of Claim 98 which additionally comprises administering at least one therapeutic agent which impedes net bone loss.

103 (new): The method of Claim 102 wherein the therapeutic agent is a bisphosphonate.

104 (new): A method for inhibiting osteoblastic metastatic growth from prostate cancer in a human comprising administering thereto a therapeutically effective amount of the hydrochloride salt of a compound of formula III



III.

105 (new): The method of Claim 104 which additionally comprises administering

an anticancer drug.

106 (new): The method of Claim 105 wherein the anticancer drug is selected from the group consisting of leuprolide, goserelin, bicalutamide, nilutamide, flutamide, vitamin D, vitamin D analogues, estrogen, estrogen analogues, prednisone, hydrocortisone, ketoconazole, cyproterone acetate, and progesterone.

107 (new): The method of Claim 104 which additionally comprises administering radiation.

108 (new): The method of Claim 104 which additionally comprises administering at least one therapeutic agent which impedes net bone loss.

109 (new): The method of Claim 108 wherein the therapeutic agent is a bisphosphonate.

Respectfully submitted,
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